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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
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09/341,119 11/18/99 SAUER

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EXAMINER

HM12/1019

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WASHINGTON DC 20004

PRATS, F	
ART UNIT	PAPER NUMBER

1651

DATE MAILED:

10/19/01

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Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

[Handwritten signature]

Office Action Summary

Application No.

09/341,119

Applicant(s)

SAUER ET AL.

Examiner

Francisco C Prats

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 14 August 2001.
- 2a) ☒ This action is FINAL. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 14-37 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 14-37 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.
- If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
 - ☐ Certified copies of the priority documents have been received in Application No. _____.
 - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
- a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

- | | |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) Paper No(s). _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ | 6) <input type="checkbox"/> Other: _____ |

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DETAILED ACTION

The amendment filed August 14, 2001, has been received and entered. The text of those sections of Title 35, U.S. Code, not included in this action can be found in a prior office action.

Claims 1-13 have been cancelled.

Claims 14-37 have been added.

Claims 14-37 are pending and are examined on the merits.

Claim Objections

The numbering of claims is not in accordance with 37 CFR 1.126 which requires the original numbering of the claims to be preserved throughout the prosecution. When claims are canceled, the remaining claims must not be renumbered. When new claims are presented, they must be numbered consecutively beginning with the number next following the highest numbered claims previously presented (whether entered or not).

Misnumbered claim 36 (second recited claim 36) has been renumbered 37.

Claim Rejections - 35 USC § 112

Claims 17 and 30 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point

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out and distinctly claim the subject matter which applicant regards as the invention.

As discussed in the previous office action, the phrase "such as" (claim 17) renders the claim indefinite because it is unclear whether the limitations following the phrase are part of the claimed invention. See MPEP § 2173.05(d).

The recitation "stucks" in claim 30 is indefinite because it is not clear what applicant means by the recitation.

Claims 14-37 are rejected under 35 U.S.C. 112, first paragraph, as failing to enable the full scope of the invention claimed, for the reasons of record set forth at pages 2-4 of the office action of February 14, 2001.

As discussed in the previous office action, the specification enables separating plasmid DNA from RNA and linear DNA by preferentially binding plasmid DNA over RNA and linear DNA to a silica support in the presence of a solution comprising 4 M potassium thiocyanate, 0.6 M NaCl, 0.1 M glycine, and 30% ethanol at a pH of 11.25 to 12.0. As also discussed in the previous office action, the specification also enables separating plasmid DNA from RNA and linear DNA by preferentially binding plasmid DNA over RNA and linear DNA to a silica support in the presence of a solution comprising 8.8 M sodium

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thiocyanate, 0.6 M NaCl, 0.1 M glycine, and 30% ethanol at a pH of 9.2 to 11.1. However, the specification does not reasonably provide enablement for using any chaotropic agent at any pH over 8 to separate plasmid DNA from RNA and linear DNA, as currently encompassed by the claims.

All of applicant's argument on this issue has been fully considered but is not persuasive of error. It is noted that claims encompassing inoperative embodiments are not necessarily considered non-enabling. However, it is respectfully submitted that the present situation requires a holding of lack of enablement, in view of the highly unpredictable nature of the subject matter claimed. As discussed in the previous office action, Gautsch et al (U.S. Pat. 6,027,750) clearly demonstrate that using certain chaotropic agents at pH 8.0, one cannot even obtain plasmid binding to glass. See Table 2, at cols. 13 and 14. See also, Boom et al, at col. 14, Example A5. Thus, Gautsch and Boom clearly demonstrate that the simple practice of binding plasmid DNA to glass or silica in the presence of a chaotropic agent is in fact a fairly unpredictable art requiring significant experimentation as to the selection and concentration of chaotropic agent, as well as the determination of suitable pH.

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As further discussed in the previous office action, the process claimed by applicant adds the additional requirement that the plasmid DNA must preferentially bind to the silica without RNA or linear DNA binding to the silica. As applicant's own examples demonstrate, this also requires significant experimentation. See specification at pages 21 and 22. Note specifically that applicant's own examples demonstrate that no binding of either plasmid or linear DNA occurs above pH 12 in the preferred binding solution, despite the fact that such a pH and solution is clearly encompassed by the current claim language. Thus, applicant's own example demonstrates that the claimed objective of preferential plasmid DNA binding cannot be achieved under all of the conditions encompassed by the claims.

In sum, it is respectfully submitted that the very high degree of unpredictability in the art clearly suggests that very specific conditions are required to practice the invention as claimed. This is underscored by the fact that embodiments encompassed by the claims clearly do not function in accordance with the preamble. It is therefore respectfully submitted that, with the exception of certain embodiments, a holding of non-enablement remains proper.

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Claim Rejections - 35 USC § 103

Claims 14-19, 21-24, 27-30 and 34 are rejected under 35 U.S.C. 103(a) as being unpatentable over Little et al (U.S. Pat. 5,075,430) and Marko et al (Anal. Biochem. 121(2):382-387 (1982)) for the reasons of record set forth at pages 7-9 of the office action of February 14, 2001.

In sum, as discussed in the previous office action, the determination of a suitable pH range for practice of Little's and Marko's process clearly would have been an obvious matter of routine optimization.

Claims 14-24 and 27-34 are rejected under 35 U.S.C. 103(a) as being unpatentable over Little et al (U.S. Pat. 5,075,430) and Marko et al (Anal. Biochem. 121(2):382-387 (1982) as applied to claims 14-18, 22-29, 34, 36 and 37 above, and in further view of Smith et al (U.S. Pat. 6,027,945) and Segel (*Biochemical Calculations*, pp. 403-406 (Appendix IV), John Wiley & Sons, Inc., New York, 1976), for the reasons of record set forth at pages 9 and 10 of the office action of February 14, 2001.

In sum, as discussed in the previous office action, the advantages of using magnetized glass particles disclosed by Smith, as well as the art-recognized equivalence of Segel's amino acid buffers, renders obvious the use of these materials.

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Claims 25, 26 and 35-37 are rejected under 35 U.S.C. 103(a) as being unpatentable over Bastian et al (WO 95/21849 or U.S. Pat. 6,180,778 B1) in view of Segel (*Biochemical Calculations*, pp. 403-406 (Appendix IV), John Wiley & Sons, Inc., New York, 1976) for the reasons of record set forth at pages 10 and 11 of the office action of February 14, 2001.

In sum, the substitution of known equivalent chaotropic agents and buffers for those known to be useful in DNA-purifying solutions clearly must be considered obvious in view of the cited references.

All of applicant's argument on the issue of obviousness has been fully considered but is not persuasive of error. It may be true that common methods of DNA purification employ the use of a relatively purified cleared lysate. However, applicant's claims only require that the starting material contain a mixture of nucleic acid species. Thus, despite the argued common use of relatively purified cleared lysates in plasmid purifications, applicant's claims encompass the processes disclosed in the prior art with respect to the materials contacted with the glass material.

In this regard Marko clearly discloses that contaminating chromosomal DNA will be present if the intervening alkali

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treatment steps are omitted from the process. See page 384.

("Steps 3 and 5 are optional and may be omitted when small amounts of contaminating chromosomal DNA or protein can be tolerated.") Thus, Marko clearly contemplates contacting the claimed starting material with the claimed agents. Moreover, Marko's Figure 1 at page 385 clearly discloses that even when the alkali digestion steps are performed there are non-plasmid nucleic acid species in the purification step immediately preceding the glass adsorption step. Note specifically lane "d" of Figure 1, which in addition to plasmid contains at least low molecular weight tRNA.

Further still, as discussed in the previous office action, Little, at col. 3, lines 44-48, explicitly discloses that in a high concentration of chaotropic agent the silica-containing diatomaceous earth used therein preferentially binds larger DNA over RNA and small DNA linkers. While certain of Little's examples are directed to purification of essentially pure nucleic acid from agarose, Little unequivocally discloses that plasmid DNA can be separated from other species by the methodology claimed, which is all that applicant's claims require. Still, further, while it is noted that claim 17 recites the use of a "bacterial lysate", that term encompasses any virtually any material obtained by lysis of bacteria. Thus,

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it is respectfully submitted that, as presently drafted, the claims simply do not differ from the prior art with respect to the starting material employed.

In sum, applicant argues that the prior art does not suggest that plasmid DNA can be isolated from relatively crude preparations by the methods of Marko and Little. However, it is respectfully pointed out that applicant's claims are not limited to the preparation of plasmid DNA from crude materials. Rather, applicant's claims require only that the starting material contain non-plasmid nucleic acid species in addition to the plasmid. The cited references clearly meet this limitation. Further still, to the extent that one might find it unexpected that the Marko/Little processes can be used with crude lysates, the broadly claimed starting material is clearly not commensurate in scope with any showing of unexpected result.

Lastly, it is respectfully submitted that the rejection of claims 25, 26 and 35-37 (formerly claims 12 and 13) over the Bastian and Segel references is not based on a prohibited ex-post-facto analysis. Rather, it is based on the accepted principle that the substitution of one known equivalent for another is *prima facie* obvious. See MPEP § 2144.06, entitled "Art Recognized Equivalence for the Same Purpose". In the instant case the prior art suggests compositions containing

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thiocyanates and buffers. Applicant's claims clearly employ a known thiocyanate and a known buffer. Absent some evidence of an unexpected result inhering from the specific ingredients recited in the claims, it is respectfully submitted that the holding of obviousness must be maintained.

No claims are allowed.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event,

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however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Francisco C Prats whose telephone number is 703-308-3665. The examiner can normally be reached on Monday through Friday, with alternate Fridays off.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Wityshyn can be reached on 703-308-4743. The fax phone numbers for the organization where this application or proceeding is assigned are 703-305-3014 for regular communications and 703-305-3014 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.



Francisco C Prats
Primary Examiner
Art Unit 1651

FCP
October 17, 2001